### **PATENT COOPERATION TREATY**

### **PCT**

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### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or age	nt's file reference		See Noti	fication of Transmittal of International	
P025931WO FOR FURT		FOR FURTHER A		ary Examination Report (Form PCT/IPEA/416)	
International application No. International fi		International filing date	day/month/year)	Priority date (day/month/year)	
PCT/GB01/04789 29/10/2001				27/10/2000	
International Pate C07K14/195	International Patent Classification (IPC) or national classification and IPC C07K14/195				
Applicant					
CHIRON S.P.	A. et al.				
This internation     and is trans	ational preliminary exam smitted to the applicant a	ination report has been according to Article 36.	prepared by this In	ternational Preliminary Examining Authority	
2. This REPO	RT consists of a total of	9 sheets, including this	s cover sheet.		
<b>⊠</b> +					
				ion, claims and/or drawings which have rectifications made before this Authority	
	ule 70.16 and Section 6				
These anne	exes consist of a total of	3 sheets.			
3. This report	contains indications rela	ating to the following iter	ns:		
ı 🗵	Basis of the report				
	Priority				
		_	ovelty, inventive ste	p and industrial applicability	
	Lack of unity of invention	*			
V 🗵	Reasoned statement un citations and explanation	nder Article 35(2) with r ons suporting such state	egard to novelty, in ement	ventive step or industrial applicability;	
VI □	Certain documents cité	·			
	Certain defects in the ir				
	Certain observations or		cation		
Date of submission of the demand		Date of completion of	of this report		
23/05/2002	23/05/2002				
	address of the internationa	ı	Authorized officer	SON SCHES FATCHES	
preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d			Marinoni, J-C	A CHARLES SAN OF	
Fax: +49 89 2399 - 4465			Telephone No. +49	89 2399 8563	

International application No. PCT/GB01/04789

I.	<b>Basis</b>	of the	report
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1.	. With regard to the <b>elements</b> of the international application (Replacement sheets which have been furnished the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally file and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)): <b>Description, pages:</b>			ort as "originally filed"			
	1-3	023	as originally filed				
	Cla	ims, No.:					
	1-2	8	as originally filed				
	Cla	ims, pages:					
	303	24-3030,3032-3037 89-3046, 88-3057	,	as originally	filed		
	303	31,3047	as received on	18/12/2002	with letter of	18/12/2002	
	303	88	as received on	24/01/2003	with letter of	24/01/2003	
	Dra	wings, sheets:					
	1/9	5-95/95	as originally filed				
	Sec	uence listing part	of the description, pages:			·	
	1-10	372, as originally fil	ed				
<ol> <li>With regard to the language, all the elements marked above were available or furnished to this Authority ir language in which the international application was filed, unless otherwise indicated under this item.</li> </ol>			o this Authority in the this item.				
	The	These elements were available or furnished to this Authority in the following language: , which is:					
		the language of a	translation furnished for the purp	ooses of the ir	nternational search (ur	nder Rule 23.1(b)).	
		the language of pu	ublication of the international app	olication (unde	er Rule 48.3(b)).		
		the language of a 55.2 and/or 55.3).	translation furnished for the purp	oses of interr	national preliminary ex	amination (under Rule	
3.	With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:						

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	$\boxtimes$	contained in the international application in written form.				
	$\boxtimes$	filed together with the international application in computer readable form.				
		furnished subseque	ntly to this Authority in written form.			
		furnished subseque	ntly to this Authority in computer readable form.			
		The statement that the international app	that the subsequently furnished written sequence listing does not go beyond the disclosure in application as filed has been furnished.			
		☐ The statement that the information recorded in computer readable form is identical to the written sequent listing has been furnished.				
4.	The	amendments have resulted in the cancellation of:				
		the description,	pages:			
		the claims,	Nos.:			
		the drawings,	sheets:			
5.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):				
		(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)				
•						
		litional observations,				
III.	<b>Nor</b>	n-establishment of o	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be non-			
III.	<b>Nor</b>	n-establishment of o	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be nonially applicable have not been examined in respect of:			
III.	Nor The obvi	n-establishment of o questions whether the ious), or to be industr the entire internatior	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be nonially applicable have not been examined in respect of:			
<b>III.</b> 1.	Nor The obvi	n-establishment of conceptions whether the ious), or to be industration the entire internation claims Nos. 19-22 co	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be nonially applicable have not been examined in respect of: all application.			
<b>III.</b> 1.	Nor The obvi □ ⊠	n-establishment of or questions whether the ious), or to be industration the entire internation claims Nos. 19-22 contents.	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be non- ially applicable have not been examined in respect of: nal application. Impletely; 17, 26 partially. I application, or the said claims Nos. 17 partially relate to the following subject matter ire an international preliminary examination (specify):			
<b>III.</b> 1.	Nor The obvi □ ⊠	n-establishment of or questions whether the ious), or to be industrated the entire internation claims Nos. 19-22 consections.  the said international which does not requise see separate sheet the description, clair	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be non- ially applicable have not been examined in respect of: nal application. Impletely; 17, 26 partially. If application, or the said claims Nos. 17 partially relate to the following subject matter irre an international preliminary examination (specify):  This or drawings (indicate particular elements below) or said claims Nos. 19-22 ally are so unclear that no meaningful opinion could be formed (specify):			
<b>III.</b> 1.	Nor The obvi □ ⊠ caus	questions whether the duestions whether the ious), or to be industrated the entire internation claims Nos. 19-22 celes.  the said international which does not requise separate sheet the description, claim completely; 26 partials see separate sheet the claims, or said celes.	pinion with regard to novelty, inventive step and industrial applicability ne claimed invention appears to be novel, to involve an inventive step (to be non- ially applicable have not been examined in respect of: nal application. Impletely; 17, 26 partially. If application, or the said claims Nos. 17 partially relate to the following subject matter irre an international preliminary examination (specify):  This or drawings (indicate particular elements below) or said claims Nos. 19-22 ally are so unclear that no meaningful opinion could be formed (specify):			

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2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleo and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrations: Instructions:						
		the written form has no	t been fi	urnished	or does not comply with the standard.	
		the computer readable	form ha	s not bee	en furnished or does not comply with the standard.	
IV.	. Lac	ck of unity of invention				
1.	ln r	In response to the invitation to restrict or pay additional fees the applicant has:				
	×	☑ restricted the claims.				
		□ paid additional fees.				
		paid additional fees under protest.				
		neither restricted nor pa	aid addit	ional fees	es.	
2.		This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.				
3.	This	This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 i				
		complied with.				
	×	not complied with for th see separate sheet	e follow	ing reaso	ons:	
4.		nsequently, the following mination in establishing			rnational application were the subject of international preliminary	
		all parts.				
	×	the parts relating to clai	ms Nos	. 1-7,9-18	8,23-28.	
V.		leasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; itations and explanations supporting such statement				
1.	Statement					
	Nov	elty (N)	Yes: No:	Claims Claims	1-7,9,10,18,27 11-17,23-26,28	
	Inve	entive step (IS)	Yes: No:	Claims Claims		
	Indu	ustrial applicability (IA)	Yes: No:	Claims Claims	1-16,18,23-28 17	

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2. Citations and explanations see separate sheet

### **EXAMINATION REPORT - SEPARATE SHEET**

#### Re Item III

### Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- Claim 22 is directed to a computer-readable medium which amounts to the mere presentation of information. Examination of such subject-matter is not required (see Article 34(4)(a)(i) and Rule 67.1(v) PCT). Moreover the subject-matter of said claim was not searched according to Rule 39.1(v) PCT. Therefore, examination of said subject-matter is not carried out in the present report.
- 2. Claim 26 is directed to subject-matter which finds no support of technical nature (Article 6 PCT) and is not sufficiently disclosed (Article 5 PCT) over the entire range claimed. Search was restricted to antibodies to the claimed proteins. Examination is carried out only for said subject-matter.
- 3. Claim 17 partially relates to treatment of the animal/human body by therapy. Examination is not required for said subject-matter (see Article 34(4)(a)(i) and Rule 67.1(iv) PCT). Examination is only carried out regarding the alleged effect of the compounds referred to in the claim.
- It is considered that the subject-matter covered by claims 19-21 is so vaguely 4. defined, that virtually any pair of primer falls into the scope of the claim, contrary to Article 6 PCT, that no examination can be carried out regarding the subjectmatter of said claims.

#### Re Item IV

#### Lack of unity of invention

- 1. The ISA raised an objection for lack of unity of the invention under Rule 13 PCT and subsequently identified more than 6500 groups of inventions. Following the payment of 3 additional search fees, the search has been restricted to the inventions of examples 1245 (SEQ ID No. 3849, 3850, 8769, 8770), 679 (SEQ ID No. 2091, 2092, 2093, 2094, 8637, 8638), 498 (SEQ ID No. 1593, 1594, 8583, 8584) and 67 (SEQ ID No. 215, 216, 217, 128).
- 2. The separate groups of invention are therefore:
  - the nucleic and amino acid sequences of example 1245 (SEQ ID No. 3849, (i)

- 3850, 8769, 8770), antibodies, compositions, processes and methods related thereto.
- (ii) the nucleic and amino acid sequences of example 679 (SEQ ID No. 2091, 2092, 2093, 2094, 8637, 8638), antibodies, compositions, processes and methods related thereto.
- (iii) the nucleic and amino acid sequences of example 498 (SEQ ID No. 1593, 1594, 8583, 8584), antibodies, compositions, processes and methods related thereto.
- (iv) the nucleic and amino acid sequences of example 67 (SEQ ID No. 215, 216, 217, 128), antibodies, compositions, processes and methods related thereto.
- 3. They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:
  - The present application relates to proteins from group B Streptococcus (S. agalactiae) and from group A Streptococcus (S. pyogenes) that are allegedly useful antigens for vaccines, immunogenic compositions and/or diagnostics, and also targets for antibiotics.
  - Proteins from group A and group B Streptococci, in particular S. agalactiae and S. pyogenes are known from the art. Therefore, two main groups of inventions are present in the application.
  - Additionally, proteins of S. agalactiae and S. pyogenes useful as antigens for vaccines, immunogenic compositions and/or diagnostics are known from the art (see inter alia D4 for S. agalactiae or D5 for S. pyogenes).
- The nucleic acids/proteins can somehow be grouped according to their sequence 4. for the reason that homologues of a given nucleic acids/proteins found in S. pyogenes were found in S. agalactiae (see the examples). However, it is still considered that these constitute separate invention since they do not share a common inventive feature, i.e. a special technical feature in the sense of Article 13 PCT. However, due to the sequence similarities, examination can be performed for each of the identified groups of inventions provided that additional fees are timely paid.
- 5. The Applicant chose not to pay additional fees and restricted the subject-matter to be examined to group of inventions (iii), i.e. claims 1-7, 9-18, 23-28 all partially.

#### Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- Cited documents
  - D1: DATABASE GENESEQ, 9 November 1998, BLACK M T ET AL.: 'Streptococcus pneumoniae polypeptide coding region' Database accession no. AAV42990 & WO 98 23631, 4 June 1998
  - D2: DATABASE EMBL, 6 May 1999, MEEHAN MC & OWEN P: 'Sequence 1 from Patent WO9801561' Database accession no. A68631 & WO 98 01561. 15 January 1998
  - **D3**: WO9916882
  - D4: MICHEL J L ET AL: 'Cloned alpha and beta C-protein antigens of group B Streptococci elicit protective immunity' INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY, vol. 59, no. 6, June 1991, pages 2023-2028
  - D5: STALHAMMAR-CARLEMALM M ET AL: 'THE R28 PROTEIN OF STREPTOCOCCUS PYOGENES IS RELATED TO SEVERAL GROUP B STREPTOCOCCAL SURFACE PROTEINS, CONFER PROTECTIVE IMMUNITY AND PROMOTES BINDING TO HUMAN EPITHELIAL CELLS' MOLECULAR MICROBIOLOGY, vol. 33, no. 1, July 1999, pages 208-219
- 2. None of the available documents discloses a protein having the sequences of SEQ ID No. 1594 or 8584, or the nucleic acids encoding them or proteins having at least 12 identical consecutive amino acids the sequences of SEQ ID No. 1594 or 8584, or nucleic acids having more than 12 consecutive identical nucleotides. Therefore, the subject-matter of claims 1-7, 9, 10, 18, 27 meets the requirements of Article 33(2) PCT concerning novelty.
- 3. D1, D2 and D3 disclose nucleic acids encoding S. pneumoniae, S. equi, S. agalactiae proteins respectively and having 54%, 53% and 63% identity respectively with the sequence of SEQ ID No. 1593, and are hybridizable thereto. The subject-matter of claims 11 and 12 is therefore not novel. Consequently, the subject-matter of claims 13-17 and 23-26 and 28 does not meet the requirements of Article 33(2) PCT concerning novelty.

- 4. The specific sequences of SEQ ID No. 1594 and 8584 appear to involve an inventive step since it is demonstrated in the present application that they induce protective immunity against S. agalactiae on the one hand and S. pyogenes on the other hand. Therefore, the subject-matter of claims 1, 7 and 18 appears to meet the requirements of Article 33(3) PCT.
- 5. It is doubtful that the proteins defined by way of a percentage of identity all solve the technical problem underlying the application, i.e. confer protective immunity against S. agalactiae or S. pyogenes. It is obvious that the specific protein of the invention are inventive since they inherently solve this technical problem, and therefore meet the requirements of Article 33(3) PCT concerning inventive step. Fragments of these proteins defined by the fact that they contain more than 12 consecutive amino acids and that they confer protective immunity (claim 3) meet the requirements of Article 33(3) PCT too for the same reason. However, the protein of claim 2 is defined only by the fact that it has at least 60% identity to the protein of SEQ ID No. 1594/8584 without any functional limitation. The scope of the claim therefore embraces proteins which do not necessarily solve the technical problem underlying the present invention, but merely solve the technical problem of providing new amino acid sequences. The provision of new amino acid sequence which do not solve a specifically identified technical problem is not inventive. Consequently, the antibodies of claim 4-5 and the nucleic acid of claim 6 do not involve an inventive step, when referring back to claim 2. The subject-matter of claim 2, 4-5 and 6 therefore does not meet the requirements of Article 33(3) PCT concerning inventive step.

The same objection applies mutatis mutandis to the subject-matter of claim 9 which is directed to nucleic acids fragments comprising at least 12 nucleotide of the SEQ ID No. 1583/8583.

As a consequence, the subject-matter of claims 10-17 and 23-28 is not inventive when referring back to any of claims 2, 4-6 or 9.

Therefore, they cannot be considered as involving an inventive step.

Consequently, the subject-matter of claims 2, 4-6, 9-17, 23-28 does not meet the requirements of Article 33(3) PCT concerning inventive step.

6. It should be made clear in the claims that the protective immunity conferred by the proteins of the invention is effective against S. agalactiae or S. pyogenes.

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10900, 10902, 10904, 10906, 10908, 10910, 10912, 10914, 10916, 10918, 10920, 10922, 10924, 10926, 10928, 10930, 10932, 10934, 10936, 10938, 10940, 10942, 10944, 10946, 10948, 10950, 10952, 10954, 10956, 10958, 10960, 10962, 10964 and 10966.

- A protein having 60% or greater sequence identity to a protein according to claim 1.
- 5 3. A protein comprising a fragment of 12 or more consecutive amino acids from an amino acid sequence selected from the group consisting of SEQ IDs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106. 108. 110. 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 10 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244. 246. 248. 250. 252. 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406, 408, 410, 412, 414, 416, 418, 420, 422, 424, 426, 15 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 562, 564, 566, 568, 570, 572, 574, 576, 578, 580, 582, 584, 586, 588, 500, 592, 594, 596, 598, 600, 602, 604, 606, 608, 610, 612, 614, 616, 618, 620, 622, 624, 626, 628, 630, 632, 634, 636, 638, 640, 642, 644, 646, 648, 650, 652, 654, 656, 20 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686, 688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 714, 716, 718, 720, 722, 724, 726, 728, 730, 732, 734, 736, 738, 740, 742, 744, 746, 748, 750, 752, 754, 756, 758, 760, 762, 764, 766, 768, 770, 772, 7\$4, 776, 778, 780, 782, 784, 786, 788, 790, 792, 794, 796, 798, 800, 802, 804, 806, 808, 810, 812, 814, 816, 818, 820, 822, 824, 826, 828, 830, 832, 834, 836, 838, 840, 842, 844, 846, 848, 850, 852, 854, 856, 858, 860, 862, 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886. 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932. 25 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, 1086, 1088, 1090, 1092, 1094, 1096, 1098, 1100, 1102, 1104, 1106, 1108, 1110, 1112, 1114, 1116, 1118, 1120, 1122, 1124, 1126, 30 1128, 1130, 1132, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, 1162, 1164, 1166, 1168, 1170, 1172, 1174, 1176, 1178, 1180, 1182, (184, 1186, 1188, 1190, 1192, 1194, 1196, 1198, 1200, 1202, 1204, 1206, 1208, 1210, 1212, 1214, 1216, 1218, 1220, 1222, 1224, 1226, 1228, 1230, 1232, 1234, 1236, 1238, 1240, 1242, 1244, 1246, 1248, 1250, 1252, 1254, 1256, 1258, 1260, 1262, 1264, 1266, 1268, 1270, 35 1272, 1274, 1276, 1278, 1280, 1282, 1284, 1286, 1288, 1290, 1292, 1294, 1296, 1298, 1300, 1302, 1304, 1306, 1308, 1310, 1312, 1314, 1316, 1318, 1320, 1322, 1324, 1326, 1328, 1330, 1332, 1334, 1336, 1338, 1340, 1342, 1344, 1346, 1348, 1350, 1352, 1354, 1356, 1358, 1360, 1362, 1364, 1366, 1368, 1370, 1372, 1374, 1376, 1378, 1380, 1382, 1384, 1386, 1388, 1390, 1392, 1394, 1396, 1398, 1400, 1402, 1404, 1406, 1408, 1410, 1412, 1414, 1416, 1418, 1420, 1422, 1424, 1426, 1428, 1430, 1432, 1434, 1436, 1438, 1440, 1442, 1444, 1446, 1448, 1450. 40 1452, 1454, 1456, 1458, 1460, 1462, 1464, 1466, 1468, 1470, 1472, 1474, 1476, 1478, 1480, 1482, 1484, 1486, 1488, 1490, 1492, 1494, 1496, 1498, 1500, 1502, 1504, 1506, 1508, 1510, 1512, 1514, 1516, 1518, 1520, 1522, 1524, 1526, 1528, 1530, 1532, 1534, 1536, 1538, 1540, 1542, 1544, 1546, 1548, 1550, 1552, 1554, 1556, 1558. 1560, 1562, 1564, 1566, 1568, 1570, 1572, 1574, 1576, 1578, 1580, 1582, 1584, 1586, 1588, 1590,

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12009, 12010, 12011, 12012, 12013, 12014, 12015, 12016, 12017, 12018, 12019, 12020, 12021, 12022, 12023 and 12024.

9. A nucleic acid molecule comprising a fragment of 12 or more consecutive nucleotides from a nucleotide sequence selected from the group consisting of SEQ IDs 1. 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 5 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 10 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411, 413, 415, 417, 419, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485, 487, 489, 491, 493, 495, 497, 499, 501, 503, 505, 507, 509, 511, 513, 515, 517, 519, 521, 523, 525, 527, 529, 531, 533, 535, 537, 15 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 561, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591. 593, 595, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 633, 635, 637, 639, 641, 643, 645, 647, 649, 651, 653, 655, 657, 659, 661, 663, 665, 667, 669, 671, 673, 675, 677, 679, 681, 683. 685. 687, 689, 691, 693, 695, 697, 699, 701, 703, 705, 707, 709, 711, 713, 715, 717, 719, 721, 723, 725, 727, 729. 731, 733, 735, 737, 739, 741, 743, 745, 747, 749, 751, 753, 755, 757, 759, 761, 763, 765, 767, 769, 771, 773, 775, 777, 20 779, 781, 783, 785, 787, 789, 791, 793, 795, 797, 799, 801, 803, 805, 807, 809, 811, 813, 815, 817, 819, 821, 823, 825, 827, 829, 831, 833, 835, 837, 839, 841, 843, 845, 847, 849, 851, 853, 855, 857, 859, 861, 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 89\$, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 25 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053. 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, 1085, 1087, 1089, 1091, 1093, 1095, 1097, 1099, 1101, 1103, 1105, 1107, 1109, [1111, 1113, 1115, 1117, 1119, 1121, 1123, 1125, 1127, 1129, 1131, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, 1159, 1161, 1163, 1165, 1167, 1169, 1171, 1173, 1175, 1177, 1179, 1181, 1183, 1185, 1187, 1189, 1191, 1193, 1195, 1197, 1199, 1201, 1203, 30 1205, 1207, 1209, 1211, 1213, 1215, 1217, 1219, 1221, 1223, 1225, 1227, 1229, 1231, 1233, 1235, 1237, 1239, 1241, 1243, 1245, 1247, 1249, 1251, 1253, 1255, 1257, 1259, 1261, 1263, 1265, 1267, 1269, 1271, 1273, 1275, 1277, 1279, 1281, 1283, 1285, 1287, 1289, 1291, 1293, 1295, 1297, 1299, 1301, 1303, 1305, 1307, 1309, 1311, 1313, 1315, 1317, 1319, 1321, 1323, 1325, 1327, 1329, 1331, 1333, 1335, 1337, 1339, 1341, 1343, 1345, 1347, 1349, 1351, 1353, 1355, 1357, 1359, 1361, 1363, 1365, 1367, 1369, 1371, 1373, 1375, 1377, 1379, 1381, 1383, 1385, 1387, 1389, 1391, 1393, 35 1395, 1397, 1399, 1401, 1403, 1405, 1407, 1409, 1411, 1413, 1415, 1417, 1419, 1421, 1423, 1425, 1427, 1429, 1431, 1433, 1435, 1437, 1439, 1441, 1443, 1445, 1447, 1449, 1451, 1453, 1455, 1457, 1459, 1461, 1463, 1465, 1467, 1469, 1471, 1473, 1475, 1477, 1479, 1481, 1483, 1485, 1487, 1489, 1491, 1493, 1495, 1497, 1499, 1501, 1503, 1505, 1507, 1509, 1511, 1513, 1515, 1517, 1519, 1521, 1523, 1525, 1527, 1529, 1531, 1533, 1535, 1537, 1539, 1541, 1543, 1545, 1547, 1549, 1551, 1553, 1555, 1557, 1559, 1561, 1563, 1565, 1567, 1569, 1571, 1573, 1575, 1577, 1579, 1581, 1583, 40 1585, 1587, 1589, 1591, 1593, 1595, 1597, 1599, 1601, 1603, 1605, 1607, 1609, 1611, 1613, 1615, 1617, 1619, 1621, 1623,

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10792, 10794, 10796, 10798, 10800, 10802, 10804, 10806, 10808, 10816, 10812, 10814, 10816, 10818, 10820, 10822, 10824, 10826, 10828, 10830, 10832, 10834, 10836, 10838, 10840, 10842, 10844, 10846, 10848, 10850, 10852, 10854, 10856, 10858, 10860, 10862, 10864, 10866, 10868, 10870, 10872, 10874, 10876, 10878, 10880, 10882, 10884, 10886, 10888, 10890, 10892, 10894, 10896, 10898, 10900, 10902, 10904, 10906, 10908, 10910, 10912, 10914, 10916, 10918, 10920, 10922, 10924, 10926, 10928, 10930, 10932, 10934, 10936, 10938, 10940, 10942, 10944, 10946, 10948, 10950, 10952, 10954, 10956, 10958, 10960, 10962, 10964 and 10966, wherein said protein confers protective immunity.

- 4. An antibody which binds to a protein according to any one of claims 1 to 3.
- 5. The antibody of claim 4, wherein said antibody, is a monoclonal antibody, a chimeric antibody, a humanised antibody, or a fully human antibody.
- 6. A nucleic acid molecule which encodes a protein according to any one of claims 1 to 3.
- 7. A nucleic acid molecule according to claim 6, comprising a nucleotide sequence selected from the group consisting of SEQ IDs 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 15 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411, 413, 415, 417, 419, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 20 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485, 487, 489, 491, 493, 495, 497, 499, 501, 503, 505, 507, 509, 511, 513, 515, 517, 519, 521, 523, 525, 527, 529, 531, 533, 535, 537, 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 561, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591, 593, 525, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 633, 635, 637, 639, 641, 643, 645, 647, 649, 651, 653, 655, 657, 659, 661, 663, 665, 667, 669, 671, 673, 675, 677, 679, 681, 683, 685, 687, 689, 691, 693, 695, 697, 699, 701, 703, 705, 707, 709, 711, 713, 25 715, 717, 719, 721, 723, 725, 727, 729, 731, 733, 735, 737, 739, 741, 743, 745, 747, 749, 751, 753, 755, 757, 759, 761, 763, 765, 767, 769, 771, 773, 775, 777, 779, 781, 783, 785, 787, 789, 791, 793, 795, 797, 799, 801, 803, 805, 807, 809, 811, 813, 815, 817, 819, 821, 823, 825, 827, 829, 831, 833, 835, 837, 839, 841, 843, 845, 847, 849, 851, 853, 855, 857, 859, 861, 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 30 . 965, 967, 969, 971, 97|3, 975, 977, 979, 981, 983, 985, 987, 989|, 991, 993, 995|, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, 1085, 1087, 1089, 1091, 1093, 1095, 1097, 1099, 1101, 1103, 1105, 1107, 1109, 1111,  $\frac{1}{2}$ 113, 1115,  $\frac{1}{2}$ 17, 1119, 1121, 1123, 1125, 1127, 1129, 1131, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, 1159, 1161, 1163, 1165, 1167, 1169, 1171, 35 1173, 1175, 1177, 1179, 1181, 1183, 1185, 1187, 1189, 1191, 1193, 1195, 1197, 1199, 1201, 1203, 1205, 1207, 1209, 1211, 1213, 1215, 1217, 1219, 1221, 1223, 1225, 1227, 1229, 1231, 1233, 1235, 1237, 1239, 1241, 1243, 1245, 1247, 1249, 1251, 1253, 1255, 1257, 1259, 1261, 1263, 1265, 1267, 1269, 1271, 273, 1275, 1277, 1279, 1281, 1283, 1285, 1287, 1289, 1291, 1293, 1295, 1297, 1299, 1301, 1303, 1305, 1307, 1309, 1311, 1313, 1315, 1317, 1319, 1321, 1323, 1325, 1327, 1329, 40